CHAPTER 3

MENISCAL REPAIR BY FIBROCARTILAGE? AN EXPERIMENTAL STUDY IN THE DOG.

This chapter has been published in the Journal of Orthopaedic Research 10: 359-370, 1992 and is reprinted with permission of the publisher.

SUMMARY

Longitudinal lesions in the avascular part of the dog's meniscus were repaired by implantation of a porous polyurethane. Ingrowing repair tissue was characterized by biochemical and immunological analysis. Histologically, repair tissue initially consisted of fibrous tissue containing type I collagen. After 3 months fibrocartilaginous tissue developed inside of the implants whereas control defects only showed fibrous repair tissue. Both type I and II collagen, the major collagen types of normal meniscal fibrocartilage, could be detected in this newly formed fibrocartilage. It is concluded that fibrocartilage resembling normal meniscal tissue is formed and that longitudinal lesions can be healed after meniscal repair by implantation of a porous polymer.

INTRODUCTION

For a long time it was believed that the knee joint menisci were useless structures without any function,[58] until Fairbank [19] called attention to the roentgenographic signs of post-meniscectomy joint degeneration which now bear his name. Since then the observation that removal of a meniscus results in degeneration of the articular cartilage has been confirmed many times.[28,30,45,59,62]

Today the functions attributed to the meniscus are primarily load bearing and stress distribution within the knee joint thus protecting the underlying articular cartilage from concentrations of stress and overloading [36,38,39,51,53,55,56] Providing joint stability may be of importance after ligamentous insufficiency [38,39,55] and also improvement of joint lubrication has been proposed as a meniscal function.[41] Leaving a meniscal tear without treatment is controversial since, apart from causing disability to the patient, meniscal lesions itself can cause degenerative changes of articular cartilage.[14,54]

In dogs it has been shown that the degree of osteoarthritis after meniscectomy is inversely related to the amount of fibrocartilage remaining.[15,34] This fact has led to a trend to preserve meniscal tissue if possible while addressing the clinical symptoms caused by tears by performing a partial meniscectomy.[23,29,43,48] Although partial meniscectomy does improve results and diminishes postmeniscectomy osteoarthritis, stresses on the underlying cartilage are still increased and therefore osteoarthritis is not prevented.[15,43,53]

Preserving all meniscal tissue when possible probably is the best option. The options then are either repair of meniscal lesions or implantation of a substitute meniscus which can replace a destroyed meniscus after total meniscectomy. Fresh, freeze-dried or glutaraldehyde preserved allografts in goats and dogs are less successful.[10,32] A cryopreserved allograft in dogs is reported to function well up to a period of 6 months, but the long-term results are unknown. Furthermore remodelling of the collagen structure and poor central ingrowth of the allograft may limit the long-term functional properties.[2,5] Both a degradable collagen prosthesis [57] and a non-degradable teflon-net prosthesis [60] in the dog are reported to provide cartilage protection by formation of a fibrocartilaginous structure whereas a polyester carbon fibre prosthesis [65] had meagre results.

Several methods have been applied for repair of meniscal lesions. Whereas Annandale in 1885 [1] was the first to repair a torn meniscus, King's experiments set the biological limitations of meniscal healing.

He showed that meniscal lesions which communicate with the synovial lining of the joint capsule may be healed by connective tissue whereas lesions limited to the semilunar cartilage do not heal.[34] The reason for the very limited healing potential of meniscal lesions is the fact that bloodvessels, necessary for healing, are present only in the peripheral 10-30% of the meniscus whereas the central part of the meniscus, where most lesions occur, is avascular.[3,4]

Repair of peripheral lesions by suturing has now been widely applied with good results in both animals like dog and monkey [9] and in humans.[11] Abrading parameniscal synovial tissue is another option to improve healing of peripheral tears.[26] For lesions in the avascular part of the meniscus repair has been attempted by creation of a radial access channel from the vascular periphery towards a lesion, but due to obstruction of this conduit improvement of vascularity is not very significant.[20,26] Repair by suturing of a synovial flap between lesion and periphery does stimulate healing but fibrous repair tissue is formed.[20]

Some procedures do result in improved healing of the tear. However, in general healing takes place by ingrowth of abnormal fibrous tissue which can also be seen in regenerated menisci.[8,9,20,24,31,35] Such fibrovascular scar tissue will have abnormal biomechanical properties and can not be expected to function adequately in the long term. Reports on repair of meniscal lesions by fibrocartilage are sparse but has been observed in spontaneously healed meniscal lesions in the rabbit [25] and after application of a fibrin clot in the dog.[7]

Previously we have shown that repair of central lesions can be achieved by implantation of a porous polymer.[63] Morphologically, chondrocytes lying in a fibrous matrix were observed which warranted us to call this tissue fibrocartilage. To the author's knowledge meniscal repair tissue has only been described in morphological terms but further characterization has never been performed.

Therefore, the aim of this study was to determine the histological, biochemical, and immunohistological nature of the meniscal repair tissue with or without implantation of a porous polymer.

MATERIALS AND METHODS

Surgery

Experiments were performed under aseptic conditions on 27 lateral menisci of adult mongrel dogs weighing 25 kg or more. Anaesthesia was accomplished by intravenous administration of penthotal (30 mg/kg) and maintained after intubation with nitrous-oxide (2:1) and halothane.

The right or left lateral meniscus (chosen at random) was approached by a lateral incision of the knee joint capsule without detachment of any ligaments. A wedge-shaped defect was created with its base at the periphery and the top reaching inwards to at least half the width of the meniscal body. Additionally a longitudinal lesion was created well within the avascular mid-substance part of both anterior and posterior horns of the meniscus. In 19 menisci an implant was sutured into the defect using 2 mersilene 2-0 sutures. The same procedure was performed without implantation of a polymer in 8 control menisci of 4 dogs. The longitudinal tear was not sutured. Fig.1 shows the procedure used.

A synovial flap on a pedicle was sutured to the periphery of the grafted or control defects to ensure good contact with synovial tissue which is believed to be the source of replacement cells. The capsule and skin were closed in layers using dexon 3-0 sutures.

The dogs were not immobilized and walking was allowed. Follow-up periods ranged from 6-52 weeks for the implant group (Table 1). Up to 20 weeks dogs were killed with intervals of 2-4 weeks, afterwards intervals were 6 weeks. Control dogs were killed after 6, 12, 24 and 48 weeks. Follow-up periods were chosen after preliminary experiments had shown that during these time periods ingrowth of fibrous tissue, subsequent transformation into fibrocartilaginous tissue and increase and maturation of fibrocartilage occurred.

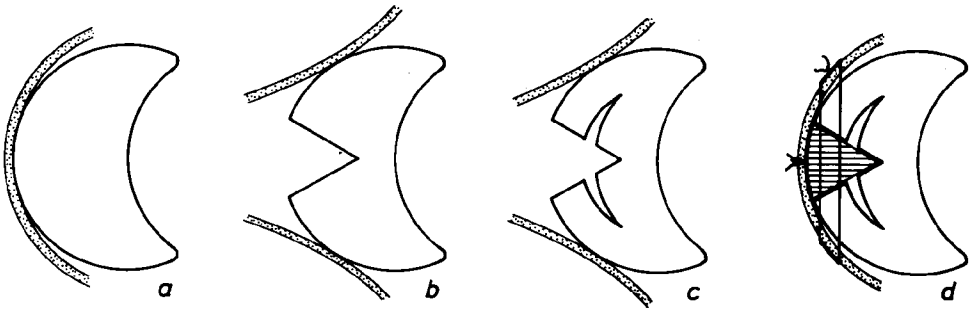

Figure 1.
A Graphical presentation of a normal lateral meniscus in the dog. The dotted structure represents the joint capsule (outer line) and synovial layer (inner line) of the knee joint.
B A wedge-shaped defect is created connecting the vascular periphery to the avascular centre of the meniscus.
C A longitudinal lesion occupying at least 30% of the meniscal length is created in the avascular part of the meniscus.
D The implant is cut to fit the defect and is sutured into place using 2 mersilene sutures. The longitudinal lesion is not sutured. A synovial flap is sutured to the periphery of the implant.

Polymer

Polymer implants consisted of a slowly degradable aliphatic polyurethane. As revealed by morphometry 50-75% is degraded after one year's follow-up. By the saltcasting / freeze-drying techniques pores were created.[16] Porosity was 86%, 31% macropores of 250-300 μm and 69% micropores smaller than 90 μm.

Histology

After sacrifice transverse sections from the implant site were taken for routine histology, biochemistry and immunohistochemistry.

Anterior and posterior horns were cut either longitudinally or transversely for assessment of healing of the longitudinal lesion. Frozen sections were taken from all menisci. Although this method allowed adequate labeling of tissue with antibodies morphology is poor since cutting of thin sections containing polymer results in tearing-out of the tough polymer. Therefore tissue was also processed for plastic embedding.[61]

Table 1. Summary of morphological findings after implantation of polymer implants and of non-implanted controls.

	6-12 weeks	14-20 weeks	24-52 weeks
Implants	*(n=3)*	*(n=7)*	*(n=7)*
Microscopic healing: (complete-partial-none)			
- anterior part of tear	2 - 0 - 1	4 - 1 - 2	5 - 1 - 1
- posterior part of tear	1 - 1 - 1	1 - 5 - 1	0 - 4 - 3
Macroscopic healing: (complete-partial-none)			
- anterior part of tear	2 - 0 - 1	4 - 1 - 2	3 - 1 - 3
- posterior part of tear	1 - 1 - 1	1 - 3 - 3	1 - 4 - 2
Degeneration of articular cartilage*	0/2	3/6	2/6
Controls	*(n=2)*	*(n=2)*	*(n=4)*
Microscopic healing: (complete-partial-none)			
- anterior part of tear	0 - 0 - 2	1 - 0 - 1	1 - 0 - 3
- posterior part of tear	0 - 0 - 2	1 - 1 - 0	0 - 0 - 4
Macroscopic healing: (complete-partial-none)			
- anterior part of tear	0 - 0 - 2	1 - 0 - 1	1 - 1 - 2
- posterior part of tear	0 - 0 - 2	1 - 0 - 1	1 - 0 - 3
Degeneration of articular cartilage*	0/2	1/2	4/4

* Degeneration of articular cartilage was examined in 14 knees with meniscal implants and in 8 knees with control defects.

Sections were fixed in acetone (-20°C), infiltrated in glycol methacrylate and embedded at 4 °C. Sections were cut at 2 μm, dried at room temperature and treated with trypsin and hyaluronidase (Sigma, St. Louis, USA) for 30 min.
When using this method we did avoid the problem of tearing-out of polymer whereas excellent labeling of collagen fibrils with improvement of morphology could be obtained.

Frozen and plastic-embedded sections were incubated with monospecific polyclonal anti-collagen I antibody (anti-human raised in goats, Southern Biotechnology Associates Inc, Birmingham, Alabama, USA) and monoclonal anti-collagen II antibody (anti-rat raised in mice) which characterization has been published before.[27] After washing and treatment with heat inactivated normal rabbit serum antibodies were applied and incubated overnight at 4 °C. The sections were incubated with peroxidase-conjugated rabbit anti-goat IgG (Dakopatts, Glostrup, Denmark) for 1 h at room temperature. Afterwards sections were incubated with DAB (Sigma) for 8 min. at room temperature. Control sections were taken through the same procedure, except that either the first or second antibody was applied. They were all negative.

Biochemistry

For biochemistry two transverse slices per implant meniscus were taken adjacent to the samples taken for light microscopy. The tissue was continuously stirred in a solution of 4 M guanidine-HCL in 0.05 M sodium acetate (Ph 5.8) at 4°C for 24 h to remove proteoglycans and stored frozen prior to analysis. After cyanogen bromide cleavage collagen types were determined by sodium SDS-gel electrophoresis.[50] Standard type I collagen was obtained from Boehringer Co. (Boehringer Mannheim Gmbh, Mannheim, Germany). Type II collagen was isolated from human articular cartilage.[37]

Articular cartilage

Femur condyles and tibia plateaus were removed and studied for gross degenerative changes. They were pencilled with India ink and studied by stereomicroscopy according to Meachim.[44]

RESULTS

Two to three weeks postoperative the dogs regained a normal gait pattern and did not seem to be hindered by the operation any more. Infections were seen in 2 implant knees, both of which had shown wound dehiscention. They were excluded from further study leaving 17 implanted menisci and 8 control defects.

Macroscopy

Up to 12 weeks the implants could easily be distinguished from normal meniscal tissue. Lateron they became completely incorporated and resembled normal meniscal fibrocartilage (Fig.2). Macroscopic examination showed considerable differences between healing of anterior and posterior parts of the longitudinal lesion. Complete healing of the anterior lesions with meniscal-like tissue was seen in two-thirds of the implant menisci whereas partial healing, defined as healing with meniscal-like without filling the lesion over the complete distance, was observed in 12% of the menisci. No healing was found in the remaining one-fourth of the menisci.

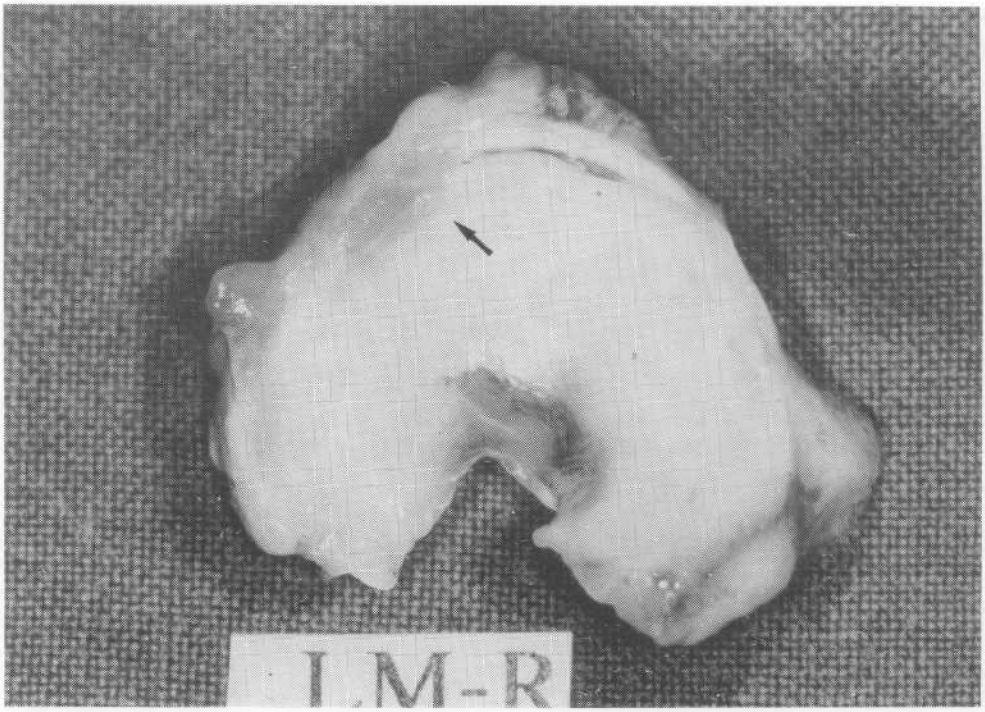

Figure 2.
A well incorporated implant after 16 weeks (x 4). The longitudinal lesion has healed. The central part of the implant is covered by fibrocartilage making it indistinguishable from normal meniscal tissue. Only the most peripheral part of the implant is still visible (arrow).

Partial healing and absence of healing was associated with partial dislocation of the implant twice. In all other cases poor direct contact between implant and meniscal fibro-cartilage existed, generally caused by a transverse gap of variable length between one side of the implant (anterior or posterior) and surrounding meniscal tissue. This gap was seen more frequently between implant and posterior horn than between implant and anterior horn, resulting in worse healing rates for lesions in the posterior horn (Table 1). Lesions classified as non-healed were either empty or filled with some abnormal fibrous-like tissue.

Healing of longitudinal lesions in control menisci was poor compared to implant menisci (Table 1). All wedge-shaped control defects remained clearly visible and were filled with soft glistening tissue.

Microscopy

Up to 12 weeks the implants were filled with vascular fibrous-like tissue. Giant cells were seen lining the polymer surface. Inside the implant pores vascular tissue containing fibroblast-like cells, macrophages and some lymphocytes was observed (Fig.3).

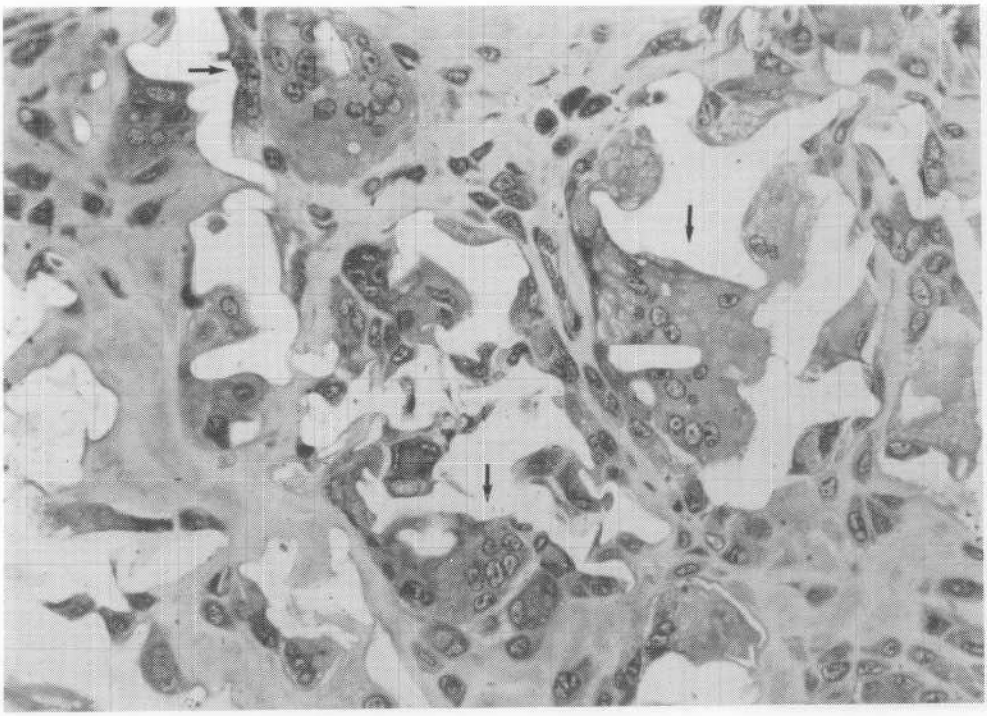

Figure 3.
Early stage of repair tissue invading the implant pores after 6 weeks follow-up (x530). Ingrowth of fibrous tissue containing capillaries, macrophages, some lymphocytes and giant cells (arrows). Polymer shown as white areas.

Wedge-shaped control defects were filled with vascular fibrous tissue without the inflammatory cells observed in the polymer group.

Labeling with anti-collagen type I antibodies showed diffuse labeling in all parts of the implant. Labeling with type II antibodies was negative. The same reaction was seen in control defects.

At 12-20 weeks the tissue reaction changed progressively for the implant group. Starting at the periphery of the implant metachromasia was observed, indicative for the formation of a cartilaginous matrix (Fig.4 and 5). In these areas chondrocytes could be observed lying in lacunae. Bloodvessels and all cell types other than meniscal-like fibrochondrocytes were absent. Labeling with type I antibodies showed diffuse labeling of both fibrous tissue and metachromatic fibrocartilage. Type II antibodies showed very specific labeling of chondrogenic areas whereas fibrous tissue did not show any labeling (Fig.6). Repair tissue in control defects still consisted of vascular fibrous tissue. Metachromasia was not observed and only type I antibodies showed diffuse labeling.

From 24-52 weeks fibrocartilage formation inside the implant group increased until the implants were completely filled with fibrocartilage. Afterwards this tissue did not change. Diffuse labeling with both type I and type II antibody was observed. Control defects still showed the same fibrous tissue reaction as seen before.

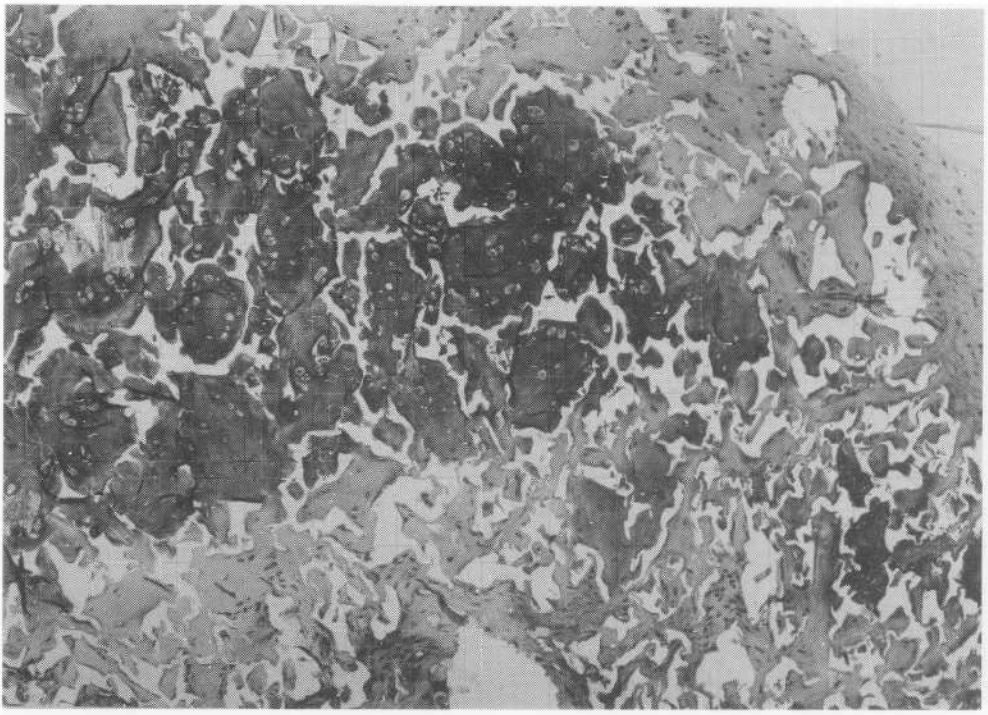

Figure 4.
Transformation of fibrous tissue into fibrocartilage (metachromasia of the dark areas) after 16 weeks. Bloodvessels and all cell types other than meniscal-like fibrochondrocytes have disappeared (x130).

Microscopically, two-thirds of longitudinal lesions in the anterior horn of the implant menisci were completely healed. Partial healing, in which only a part of the tear was filled with repair tissue was seen in 2 of 17 anterior tears whereas no healing was found in one quarter of the anterior tears (table 1). For tears in the posterior horn complete healing (2/17) was rare whereas partial healing (10/17) and lack of healing (5/17) was seen more frequently. Up to 12 weeks repair tissue inside the tear consisted of fibrous tissue, afterwards this tissue transformed into fibrocartilage, similar to the reaction observed inside the implants (Fig.7).

The longitudinal lesions of control defects were empty up to 12 weeks (Fig.8). Afterwards a minority of tears in both anterior and posterior horn were filled with vascular fibrous tissue which did not show any transformation into fibrocartilaginous tissue as could be observed in implant menisci. Macroscopic and microscopic healing rates were not always the same. It appeared that healing of a number of tears was not throughout the entire thickness of the tear. A tear could show healing at the surface (classified as macroscopic healing) whereas the deeper parts were not healed (classified as microscopic non-healing) and vice versa. Progression of healing of a tear, rendering partially healed tears into completely healed ones was not obvious from the follow-up periods chosen.

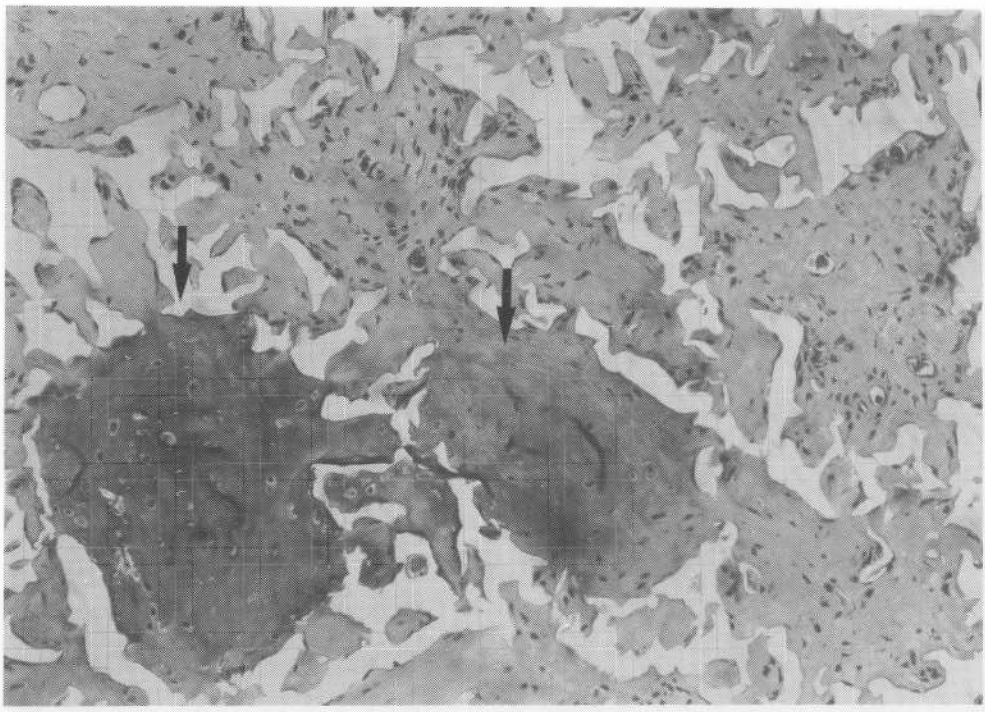

Figure 5.
Fibrocartilage formation is a focal process. In a 12 weeks' implant areas of fibrocartilage formation (arrows) are surrounded by fibrous tissue which has not yet transformed into fibrocartilage (x210).

Biochemistry

Biochemical analysis of the tissue inside the implants confirmed the transition of collagen types observed after labeling with antibodies. When only fibrous tissue was seen microscopically the presence of type I collagen was 100% without any detectable type II collagen. When repair tissue became metachromatic the amount of type I collagen decreased and type II collagen could be detected. In long-term implants completely filled with fibrocartilage type I collagen decreased to a minimum of 11% and type II collagen increased to a maximum of 89% (Table 2).

Articular cartilage

Osteoarthritis of cartilage was observed in 5 of 14 examined implant knees (36%), three times before a follow-up of 20 weeks, once after 34 weeks and once after 52 weeks. In all these knees poor healing of meniscus (3 times) or dislocation of implant (2 times) was observed. Degenerative changes were only present on the lateral tibia plateau whereas the femoral condyles and medial compartments were intact.

Table 2. Summary of characterization of repair tissue after implantation of polymer implants and of non-implanted controls.

	6-12 weeks	14-20 weeks	24-52 weeks
Implants	*n=3*	*n=7*	*n=7*
Morphology repair tissue	fibrous	fibrous + fibrocartilage	fibrocartilage
Type I collagen			
-Labeling	positive	positive	positive
-Biochemistry (±12%)	100%	31-37%	11-20%
Type II collagen			
-Labeling	negative	positive	positive
-Biochemistry (±5%)	0%	63-69%	80-89%
Controls	*n=2*	*n=2*	*n=4*
Morphology repair tissue	fibrous	fibrous	fibrous
Type I collagen			
-Labeling	positive	positive	positive
Type II collagen			
-Labeling	negative	negative	negative

There did not seem to be a relationship to follow-up time, healing of tear or cartilage formation inside the implant. In control defects degenerative changes were first noticed after 12 weeks and increased with increasing follow-up. Of 8 examined knees two-thirds showed signs of degeneration.

DISCUSSION

Meniscal lesions in the avascular part of the dog's meniscus were repaired by implantation of a porous polyurethane implant after which analysis of repair tissue was carried out. Two important factors concerning meniscal healing were found. Firstly, we observed that longitudinal lesions in the avascular part of the meniscus can be repaired by implantation of a porous polymer in a substantial number of cases.

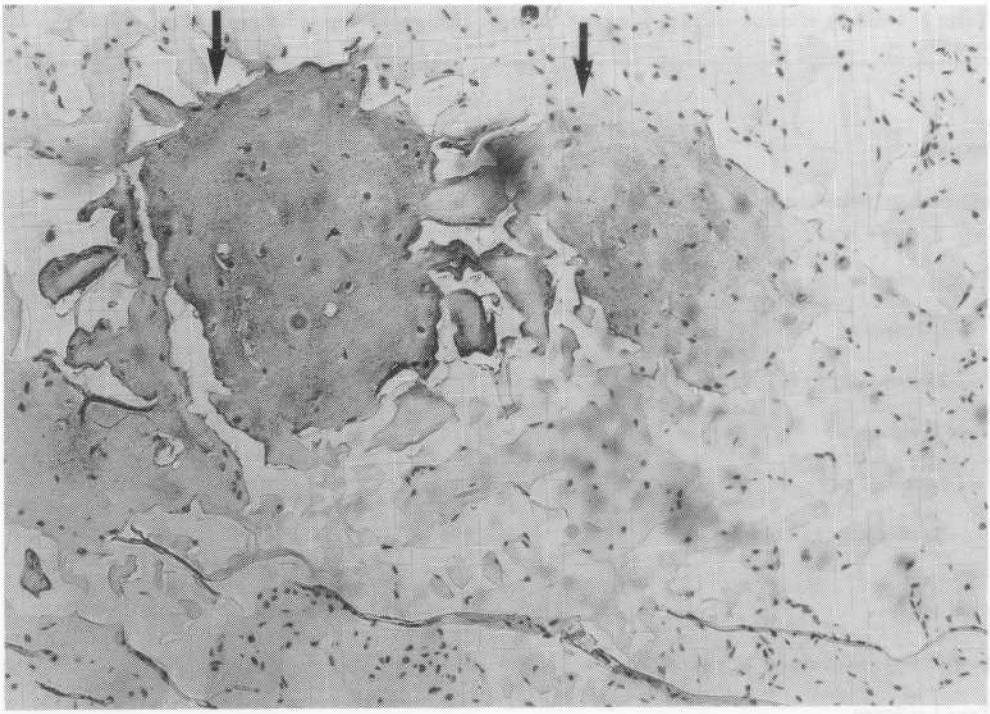

Figure 6.
Adjacent section of the one shown in figure 5. Labeling of type II collagen is observed only in areas where fibrocartilage has formed (arrows). No labeling is observed in the surrounding fibrous tissue (x210).

Secondly, it was found that the repair tissue is not the fibrous tissue observed in empty control defects but rather fibrocartilage. This is based on morphological grounds as well as on the fact that the repair tissue contains the two most important meniscal collagens type I and type II.

Meniscal fibrocartilage is a distinct tissue with special mechanical properties concerning tensile strength and compression. In general the structural and functional properties are in between those of dense connective tissue and hyaline articular cartilage. Morphologically, it can be defined as a tissue with coarse fibrous collagen bundles with fibrochondrocytes lying in between. It is believed that these cells are of chondrocyte origin. Some fibroblasts are present in the periphery and an intermediate cell type is described.[21,22] Both in bovine and human meniscal tissue biochemical collagen typing revealed that the vast majority of collagen consists of type I which is typical for tissue resisting tear forces. Type II collagen, which is the major type in articular cartilage, is only present in minor amounts.[12,17,18] A differentiation must be made concerning inner and outer part of the meniscus. Histologically, the inner one-third of the meniscus more closely resembles hyaline cartilage whereas the outer two-thirds are more fibrous in appearance.[49] The major collagen type of this inner rim is type II whereas the peripheral part of the meniscus is almost completely composed of type I collagen.[12] In addition to type I and II collagen small amounts of type III, V and VI are detectable.[12,17,18,42]

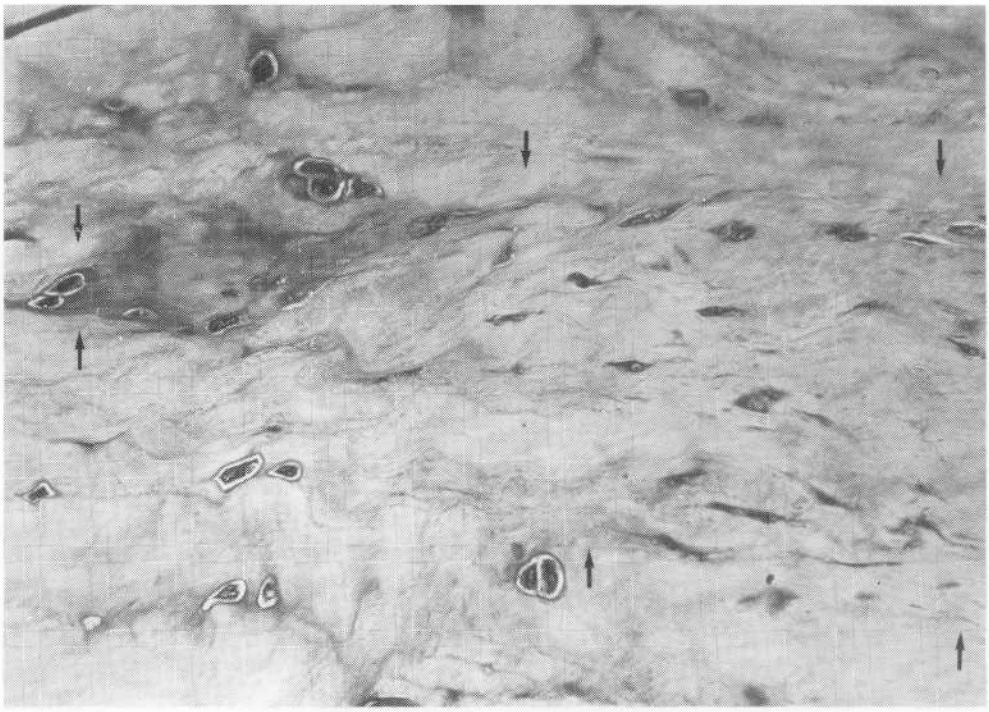

Figure 7.
Healing of longitudinal tear in a 12 weeks' implant with fibrocartilage containing chondrocytes lying in lacunae (x510). Arrows indicate the transition zone between repair tissue and meniscal fibrocartilage.

Shortly after implantation the implant became filled with vascular fibrous tissue with some inflammatory cells usually observed after implantation of a foreign body. After 2-3 months differences in the repair reaction between implant and control menisci became evident. Whereas repair tissue in control defects remained fibrous in nature, the implant favoured the development of fibrocartilage. Metachromasia of fibrous tissue was observed, chondrocyte-like cells were formed and collagen type II was found. Up to one year after operation this tissue was preserved.

The observed tissue reaction resembles the one observed in developing fibrocartilage. In the developing glans penis of the rat firstly only type I collagen is present in the mesenchymal mass. When mature chondrocytes appear and mature fibrocartilage is formed type II collagen can be detected in the extracellular matrix.[47] Why the implant stimulates fibrocartilage formation with type II collagen is not clear and to the author's knowledge this has not been described before. It seems likely that the polymer used is not the only factor responsible for this phenomenon. Other biocompatible implants which remain in situ long enough and possess an adequate physical structure and biomechanical properties may elicit this metaplasia into fibrocartilage also. The importance of these parameters is not known.

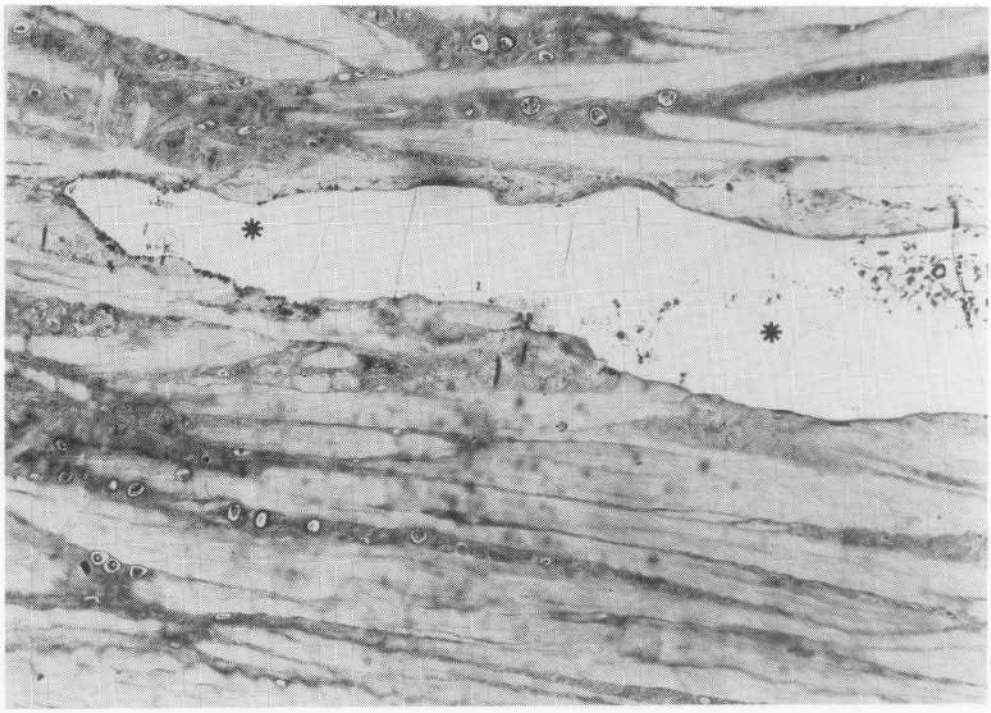

Figure 8.
Non-healed tear in a 24 weeks' implant (asterisks). No cellular reaction is observed in the surrounding meniscal tissue (x210).

Although the ultimate tissue formed strongly resembles normal meniscal fibrocartilage morphologically, the high ratio of collagen II compared to collagen I showed that the ultimate tissue formed more closely resembles the fibrocartilage present in the meniscal inner margin than that of the outer margin. Therefore it may not be concluded that normal meniscal fibrocartilage is formed. More samples will be needed for biochemical analysis of the repair tissue, paying special attention to the spatial arrangement of the repair tissue in the implant. Also biomechanical tests are needed to assess the functional properties of the repair tissue although these preliminary results seem to indicate that cartilage protection can be provided.

The origin of the repair tissue is not entirely certain. Although fibrochondrocytes can proliferate in vitro [64] and proliferative fibrocartilage cells can be found in protruding intervertebral disk material removed by operation,[40] it is generally believed that fibrocartilage cells are normally incapable of repair. Healing depends on ingrowth of fibrous tissue generated by mesenchymal progenitor cells derived from synovium or peripheral vasculature.[7,25,34] Previous experimental work has shown that the synovium is essential for regeneration of removed menisci in rabbits.[33] It is likely that compression and joint movement are necessary for metaplasia of fibrous tissue into fibrocartilage.[25,46,52] Compression may also influence the collagen type formed as can be observed in the intervertebral disk.

The upright posture of humans is thought to be the explanation for the fact that the annulus fibrosus of the intervertebral disk of humans contains much more collagen type II than can be observed in the pig.[17] The reaction also shows some similarity to the normal development of menisci after birth. Chondrogenesis follows a marked decline in vascularity, cellularity decreases and the collagen content increases. Metaplasia from fibrous tissue is observed.[13] No clustering of fibrochondrocytes or increase in cells was observed at the margins of the defect as was seen by Heatley in the rabbit.[25] This phenomenon however, was not observed by King and Arnoczky in the dog [6,34] thus it is most likely that repair cells come from outside the meniscus.

In the anterior meniscal horn two-thirds of the longitudinal tears were completely healed. For the posterior horn complete healing was less frequent but more than half of the tears did show partial healing. It appeared that the best healing took place at places where implant and tear were in close contact, i.e. at the top of the wedge-shaped defect. Healing was worse in parts of the lesion more remote from these contact areas. It seems therefore that direct contact between implant and lesion favours healing. Poor healing was strongly associated with lack of contact between implant and meniscus, usually due to a gap between posterior horn and implant. The circumferential tension forces generated in the meniscus by loading may be responsible for this gap, suggesting that the surgical technique used is too traumatizing. The circumferential collagen fibers are destroyed and adequate healing is hindered by the slowly degrading implant. Implantation of a faster degrading implant may solve this problem. Results may also improve when the procedure is performed without creation of a full-thickness defect. Instead a partial-thickness defect could be created leaving the inferior meniscal surface intact. We believe that more contact between lesion and implant is necessary. This could be achieved by connecting the longitudinal tear to the periphery of the joint by using a rectangular defect instead of a wedge-shaped one. Progression of healing of a tear, rendering partially healed tears into completely healed ones was not obvious from the follow-up periods chosen. It seems more likely that a time-dependent healing rate is only present for follow-up periods up to about three months. After that time no further increase in ingrowth of tissue into the tear is noticed although for implant menisci the tissue filling the tear does show metaplasia into fibrocartilaginous tissue.

One-third of the implant knees examined showed signs of cartilage degeneration. The osteoarthritic changes were comparable to control knees and were more prominent on the tibial plateau than on the femoral plateaus possibly because frictional forces are larger on the tibia.[25] Poor healing and dislocation of implant seemed to be responsible for these changes. Degenerative changes did not increase when follow-up increased as usually is the case after meniscectomy both in the rabbit [54] and in the dog [14] where osteoarthritis is seen within 2-4 months. In control knees degenerative changes were more frequent and increased when follow-up periods were longer.

It seems therefore that a well healed meniscus by implantation of the polymer provides protection to the articular cartilage. Although meniscal lesions in the avascular part of the meniscus can be healed by implantation of porous polymers, many factors may influence the ultimate repair tissue formed. The importance of factors like physical structure of the implants as well as chemical and physical properties still have to be determined.

REFERENCES

1 Annandale T: An operation for displaced semilunar cartilage. Br Med J 1: 779, 1885.
2 Arnoczky SP, O'Brien SJ, DiCarlo EF, Warren RF, Stone K: Cellular repopulation of deep-frozen meniscal autografts - An experimental study in the dog. Trans Orthop Res Soc 13: 145, 1988.
3 Arnoczky SP, Warren RF: The microvasculature of the meniscus and its response to injury. An experimental study in the dog. Am J Sports Med 11: 131-141, 1983.
4 Arnoczky SP, Warren RF: Microvasculature of the human meniscus. Am J Sports Med 10: 90-95, 1982.
5 Arnoczky SP, Warren RF, McDevitt CA: Meniscal replacement using a cryopreserved allograft. Clin Orthop Rel Res 252: 121-128, 1990.
6 Arnoczky SP, Warren RF, Kaplan N: Meniscal remodelling following partial meniscectomy - An experimental study in the dog. Arthroscopy 1: 247-252, 1985.
7 Arnoczky SP, Warren RF, Spivak JM: Meniscal repair using an exogenous fibrin clot: An experimental study in dogs. J Bone Joint Surg 70A: 1209-1217, 1988.
8 Bruce J, Walmsley R: Replacement of the semilunar cartilages of the knee after operative excision. Br J Surg 25: 17-28, 1937.
9 Cabaud HE, Rodkey WG, Fitzwater JE: Medial meniscus repairs: An experimental and morphological study. Am J Sports Med 19: 129-134, 1981.
10 Canham W, Stanish W: A study of the biological behaviour of the meniscus as a transplant in the medial compartment of a dog's knee. Am J Sports Med 14: 376-379, 1986.
11 Cassidy RE, Shaffer AJ: Repair of peripheral meniscus tears: A preliminary report. Am J Sports Med 9: 209-214, 1981.
12 Cheung HS: Distribution of type I, II, III, and V collagen in the pepsin solubilized collagens in bovine menisci. Connect Tiss Res 16: 343-356, 1987.
13 Clark CR, Ogden JA: Development of the menisci in the human knee joint. J Bone Joint Surg 65A: 538-547, 1983.
14 Cox JS, Cordell LD: The degenerative effects of medial meniscus tears in dogs' knees. Clin Orthop Rel Res 125: 236-242, 1977.
15 Cox JS, Nye CE, Schaefer WW, Woodstein IJ: The degenerative effect of partial and total resection of the medial meniscus in dogs' knees. Clin Orthop Rel Res 109: 178-183, 1975.
16 de Groot JH, Nijenhuis AJ, Bruin P, Pennings AJ, Veth RPH, Klompmaker J, Jansen HWB: The use of porous biodegradable polymer implants in meniscus reconstruction. 1. Preparation of porous biodegradable polyurethanes for the reconstruction of meniscus lesions. Colloid Polym Sci 268: 1073-1081, 1990.
17 Eyre DR, Muir H: Quantitative analysis of types I and II collagens in human intervertebral disks at various ages. Biochem Biophys Acta 492: 29-42, 1977.
18 Eyre DR, Wu JJ: Collagen of fibrocartilage: A distinctive phenotype in bovine meniscus. FEBS Lett 158: 265-270, 1983.
19 Fairbank TJ: Knee joint changes after meniscectomy. J Bone Joint Surg 30B: 664-670, 1948.
20 Gershuni DH, Skyhar MJ, Danzig LA, Camo J, Hargens AR, Akeson WH: Experimental models to promote healing of tears in the avascular segment of canine knee menisci. J Bone Joint Surg 71A: 1363-1370, 1989.
21 Ghadially FN, Lalonde JMA, Wedge JH: Ultrastructure of normal and torn menisci of the human knee joint. J Anat 136: 773-791, 1983.
22 Ghadially FN, Thomas I, Young N, Lalonde J-MA: Ultrastructure of rabbit semilunar cartilages. J Anat 125: 499-517, 1978.
23 Hargreaves DJ, Seedhom BB: On the bucket handle tear: Partial or total meniscectomy? A quantitative study. J Bone Joint Surg 61B: 381, 1979.
24 Hashimoto J, Kurosaka M, Yoshiya S, Hirohata K, Saura R, Matsubara T: Meniscal repair using fibrin glue and endothelial cell growth factor (ECGF) - An experimental study in dogs. Trans Orthop Res Soc 15: 562, 1990.
25 Heatley FW: The meniscus - Can it be repaired? An experimental investigation in rabbits. J Bone Joint Surg 62B: 397-402, 1980.
26 Henning CE, Lynch MA: Vascularity for healing of meniscus repairs. Arthroscopy 3: 13-18, 1987.
27 Holmdahl R, Andersson M, Tarkowski A: Origin of the autoreactive anti-type II collagen response. I.Frequency of specific and multispecific B cells in primed murine lymph nodes. Immunology 61: 369-374, 1987.
28 Huckell JR: Is meniscectomy a benign procedure? A long-term follow-up study. Can J Surg 8: 252-260, 1965.

29 Jackson RW, Dandy DJ: Partial meniscectomy. J Bone Joint Surg 58B: 142, 1976.
30 Johnson RJ, Kettelkamp DB, Clark W, Leaverton P: Factors affecting late results after meniscectomy. J Bone Joint Surg 56A: 719-729, 1974.
31 Kawai Y, Fukubayashi T, Nishino J: Meniscal suture An experimental study in the dog. Clin Orthop Rel Res 243: 286-293, 1989.
32 Keating EM, Malinin TI, Belchic G: Meniscal transplantation in goats: An experimental study. Trans Orthop Res Soc 13: 147, 1988.
33 Kim JM, Moon MS: Effect of synovectomy upon regeneration of meniscus in rabbits. Clin Orthop Rel Res 141: 287-294, 1979.
34 King D: The function of semilunar cartilages. J Bone Joint Surg 18: 1069-1076, 1936.
35 King D: Regeneration of the semilunar cartilage. Surg Gynecol & Obstet 36: 167-170, 1936.
36 Krause WR, Pope MH, Johnson RJ, Wilder DG: Mechanical changes in the knee after meniscectomy. J Bone Joint Surg 58A: 599-604, 1976.
37 Kuijer R, van de Stadt RJ, Koning MHMT, van der Korst JKL: Influence of constituents of proteoglycans on type II collagen fibrillogenesis. Collagen Rel Res 5: 379-391, 1985.
38 Levy IM, Torzilli PA, Gould JD, and Warren RF: The effect of lateral meniscectomy on motion of the knee. J Bone Joint Surg 71A: 401-406, 1989.
39 Levy IM, Torzilli PA, Warren RF: The effect of medial meniscectomy on anterior-posterior motion of the knee. J Bone Joint Surg 64A: 883-888, 1982.
40 Lipson SJ: Metaplastic proliferative fibrocartilage as an alternative concept to herniated intervertebral disk. Spine 13: 1055-1060, 1988.
41 MacConaill MA: The movement of bones and joints. 3. The synovial fluid and its assistants. J Bone Joint Surg 30B: 244-252, 1950.
42 McDevitt CA, Webber RJ: The ultrastructure and biochemistry of meniscal cartilage. Clin Orthop Rel Res 252: 8-18, 1990.
43 McGinty JB, Geuss LF, Marvin RA: Partial or total meniscectomy A comparative analysis. J Bone Joint Surg 59A: 763-766, 1977.
44 Meachim G: Light microscopy of indian ink preparations of fibrillated cartilage. Ann Rheum Dis 31: 457-464, 1972.
45 Medlar RC, Mandiberg JJ, Lyne ED: Meniscectomies in children Report of long-term results (mean 8.3 years) of 26 children. Am J Sports Med 8: 87-92, 1980.
46 Mooney V, Ferguson AB: The influence of immobilization and motion on the formation of fibrocartilage in the repair granuloma after joint resection in the rabbit. J Bone Joint Surg 48A: 1145-1155, 1966.
47 Murakami R: Immunohistochemical and immunoblot analysis of collagens in the developing fibrocartilage in the glans penis of the rat. Acta Morphol Neerl-Scand 25: 279-282, 1987.
48 Northmore-Ball MD, Dandy DJ, Jackson RW: Arthroscopic open partial and total meniscectomy. A comparative study. J Bone Joint Surg 65B: 400-404, 1983.
49 O'Connor BL: The histological structure of dog knee menisci with comments on its possible significance. Am J Anat 147: 407-416, 1976.
50 O'Driscoll, SW Salter, RB Keeley FW: A method for quantitative analysis of ratios of types I and II collagen in small samples of articular cartilage. Anal Biochem 145: 277-285, 1985.
51 Radin EL, De Lamotte F, Maquet P: Role of the menisci in the distribution of stress in the knee. Clin Orthop Rel Res 185: 290-294, 1984.
52 Scapinelli R, Little K: Observations on the mechanically induced differentiation of cartilage from fibrous tissue. J Pathol 101: 85-91, 1970.
53 Seedhom BB, Hargreaves DJ: Transmission of the load in the knee joint with special reference to the role of the menisci. Part II: Experimental results discussion and conclusions. Eng Med 8: 220-228, 1979.
54 Shapiro F, Glimcher MJ: Induction of osteoarthrosis in the rabbit knee joint: Histologic changes following meniscectomy and meniscal lesions. Clin Orthop Rel Res 147: 287-295, 1980.
55 Shoemaker SC, Markolf KL: The role of the meniscus in the anterior-posterior stability of the loaded anterior cruciate-deficient knee. Effects of partial versus total excision. J Bone Joint Surg 68A: 71-79, 1986.
56 Shrive NG, O'Connor JJ, Goodfellow JW: The weight bearing role of the menisci of the knee. J Bone Joint Surg 56B: 381, 1974.
57 Stone KR, Rodkey WG, Webber RJ, McKinney L, Steadman JR: Future directions collagen-based prosthesis for meniscal regeneration. Clin Orthop Rel Res 252: 129-135, 1990.

58 Sutton JB: In: Ligaments, their nature and morphology, London, Great Britain, Lewis and Co, 2nd ed, 1897.
59 Tapper EM, Hoover NW: Late results after meniscectomy. J Bone Joint Surg 51A: 517-526, 1969.
60 Toyonaga T, Uezaki N, Chikama H: Substitute meniscus of teflon-net for the knee joint of dogs. Clin Orthop Rel Res 179: 291-297, 1983.
61 van Goor H, Fidler V, Weening JJ, Grond J: Determinants of focal and segmental glomerulosclerosis in the rat after renal ablation. Evidence for macrophages and lipids. Lab Invest: 64: 754-765, 1991.
62 Veth RPH: Clinical significance of knee joint changes after meniscectomy. Clin Orthop Rel Res 198: 56-60, 1985.
63 Veth RPH, Jansen HWB, Leenslag JW, Pennings AJ, Hartel RM, Nielsen HKL: Experimental meniscal lesions reconstructed with a carbon fibre polyurethane-poly-(L-lactide) graft. Clin Orthop Rel Res 202: 286-293, 1986.
64 Webber RJ, Harris MG, Hough AJ: Cell culture of rabbit meniscal fibrochondrocytes: Proliferative and synthetic response to growth factors and ascorbate. J Orthop Res 3: 36-42, 1985.
65 Wood DJ, Minns RJ, Strover A: Replacement of the rabbit medial meniscus with a polyester - carbon implant. Biomaterials 11: 13-16, 1990.